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REMARKS/ARGUMENTS

This amendment is supplemental to the amendment filed November 10, 2005, which was fully responsive to the non-final Office Action mailed April 21, 2005. This amendment is also supplemental to amendments filed April 3, 2006, May 18, 2006 and July 21, 2006.

In this response claim 25 is amended, claims 10, 19-33, 39-43, and 47-70 are cancelled without prejudice to future prosecution, and claims 71-78 are added. The claim amendment and added claims add no new matter, and find support in the specification as outlined generally in Section I, below.

In the most recent action on the merits, the non-final Office Action dated April 21, 2005, compliance with the written description requirement of 35 U.S.C. §112 was discussed at length. To expedite prosecution, a brief discussion of the written description requirement, as it applies to the instant claims, is presented in Section II below.

The April 21, 2006, action also included rejections based on the judicially created doctrine of obviousness-type double patenting. Upon indication that claims are otherwise allowable, Applicants will provide terminal disclaimers to resolve double-patenting rejections, if appropriate.

For the convenience of the Office, Applicants will file a supplemental information disclosure statement under separate cover.

Section I. New claims 71-78, and amended claim 25, are supported by the specification as filed.

New claims 71-78 are directed to compositions that contain a nucleic acid encoding all or a fragment of hTRT, where administration of the composition elicits an adaptive immune response. Support for the claims is replete in the specification.[1]

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[1] Support for the claims is found throughout the specification, and reference herein to specific sections of the specification is not intended to imply that support for the claims is limited to those sections.

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For example, the specification includes abundant description of the hTRT protein, fragments, variants, fusion proteins, and nucleic acids encoding the foregoing polypeptides. The use of hTRT protein, fragments, variants, and fusion proteins to elicit an adaptive immune response is described at, for example, page 90, lines 13-23; page 64, lines 10-28; Example 6 (beginning on page 158 of the specification); Example 8 (beginning on page 176 of the specification); page 144, lines 19-22; and elsewhere in the specification. The use of a nucleic acid encoding an hTRT polypeptide of interest to elicit an immune response is described at page 90, lines 13-23 the specification.

Independent claims 71, 72 & 73

Each of claims 71-73 is directed to a composition that contains a nucleic acid encoding a polypeptide comprising hTRT sequence. In each case, the composition elicits an immune response against hTRT (SEQ ID NO:2).

In Claim 71 the polypeptide is the full-length hTRT protein. Thus, the nucleic acid encodes a polypeptide antigen that elicits an immune response against itself. Support for claim 71 is found at, e.g., page 37, lines 3-23 and page 90, lines 13-23.

In Claim 72 the polypeptide *comprises* SEQ ID NO:2 and can include additional amino acid segments at one or both termini (e.g., the polypeptide may be a fusion protein). Note that although the nucleic acid of claim 72 may encode non-hTRT sequence as well as SEQ ID NO:2, the claim specifies that the immune response is to a protein having the sequence of SEQ ID NO:2. Description of fusion proteins comprising all or a fragment of Seq. ID NO:2 is replete in the specification (see, e.g., page 37, lines 15-23; page 64, lines 25-28; and pages 158-174). Additional segments can include, for illustration, sequences such as the keyhole limpet hemaocyanin sequence (KLH), described at page 64, lines 25-28, or similar carrier proteins well known in the art.

In Claim 73 the polypeptide comprises a sequence at least 98% identical to SEQ ID NO:1. Support for this claim is found, *inter alia*, at page 37, lines 3-23:

> "The invention provides a wide variety of hTRT proteins useful for . . . induction of an anti-hTRT immune response . . . In one

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> embodiment, the hTRT protein of the invention is a polypeptide having a sequence of SEQ ID NO:2 . . . or a fragment thereof. . . . In another embodiment, the hTRT polypeptide differs from SEQ ID NO:2 by internal deletions, insertions, or conservative substitutions of amino acid residues. In a related embodiment, the invention provides hTRT polypeptides with substantial similarity to SEQ ID NO:2".

As noted at page 148, lines 3-6 of the specification, "polypeptides with substantial sequence identity may be 98% to 100% identical" (i.e., have a sequence at least 98% identical).[2] Also see the specification at page 64, lines 23-24 (immunogenic polypeptides usually will " . . . have substantial sequence identity to all or a contiguous portion of the amino acid sequence of the protein of SEQ. ID. NO: 2"). One of skill would expect a polypeptide with at least 98% sequence identity to SEQ ID NO:2 to elicit an immune response against hTRT (having 100% sequence identity to SEQ ID NO:2). The claimed composition is required to elicit an adaptive immune response to SEQ ID NO:2.

Independent claims 74, 75 & 76

Each of claims 74-76 is directed to a composition that contains a nucleic acid encoding a polypeptide having *at least* 10 contiguous amino acids of SEQ. ID NO:2. In each case, the composition elicits an immune response against hTRT (SEQ ID NO:2). These claims find support in the specification. Page 64, lines 20-28, discloses that peptides of "at least 10 amino acids" and having "substantial sequence identity to all or a contiguous portion of the amino acid sequence of the protein of SEQ ID NO:2" may be used as immunogens. In addition, at page 90 lines 13-23, the specification explains that administration of "naked DNA" encoding the polypeptides can be used to elicit an immune response, and states that "exemplary immunogenic hTRT peptides and

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[2] The terms *substantial similarity* and *substantial sequence identity* are equivalent (see the specification at page 149, lines 17-19, "As will be apparent to one of skill, the terms "substantial identity", "substantial similarity" and "substantial sequence identity" can be used interchangeably with regard to polypeptides or polynucleotides").

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polypeptides are described . . . in Examples 6 and 8." Example 8 describes short polypeptides (comprising from 23 to 27 contiguous residues of SEQ ID NO:2 plus an additional amino terminal cysteine) used to elicit an immune response to hTRT (see, e.g., page 176, lines 5-25). Accordingly, an immunogenic composition containing a DNA encoding consisting of at least 10 contiguous amino acids of SEQ. ID NO:2 is supported in the specification.

Independent claim 77

Claim 77 is directed to a composition containing a nucleic acid encoding a polypeptide consisting of the amino acid sequence of SEQ ID NO:2 or an immunogenic fragment thereof, where the composition, when administered to a subject, induces an adaptive immune response against hTRT (SEQ ID NO:2). Support for claim 77 is found in the sections of the specification discussed above in the discussion of claims 71-76.

Independent claims 25 (amended) and 78

As amended, Claim 25 specifies that the nucleic acid encodes an immunogenic fragment of SEQ. ID NO:2 fused to an amino acid sequence (sometimes referred to as a "carrier protein") that enhances the adaptive immune response to said fragment of SEQ. ID NO:2. As noted above, support for fusion proteins generally is found throughout the specification (see, e.g., page 37, lines 3-23 "The invention provides a wide variety of hTRT proteins useful for . . . induction of an anti-hTRT immune response . . . In one embodiment, the hTRT protein of the invention is a polypeptide having a sequence of SEQ ID NO:2 . . . or a fragment thereof. . . . The invention further provides hTRT polypeptides that are modified, relative to the amino acid sequence of SEQ ID NO:2, in some manner, e.g., truncated, mutated, derivatized, *or fused to other sequences (e.g., to form a fusion protein)*" (emphasis added). A fusion polypeptide having a fragment of SEQ ID NO:2 (hTRT) fused to a sequence that *enhances an immune response* is found at page 64, lines 25-28, describing a fusion of hTRT sequence with the carrier protein keyhole limpet hemaocyanin sequence (KLH).

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Section II. The Written Description Requirement Does Not Require Disclosure of Precise Structure For Generic DNA-Related Claims

In determining compliance with the written description requirement, the Office is guided, in part, by the Written Description Guidelines. 66 Fed. Reg. 1099 (2001). The Guidelines were based on the Federal Circuit's precedent on written description, including *The Regents of the University of California v. Eli Lilly*. Since 2001, the Federal Circuit has referred to the written description guidelines with approval (e.g., in *Enzo Biochem Inc., v. Gen-Probe Inc.*, 323 F.3d 956, 964 (Fed. Cir. 2002). In considering inventions pertaining to DNA, the Federal Circuit, adopting the language from the Guidelines, has stated the description requirement is met by "sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." *Monsanto Co. v. Scruggs*, 2006 U.S.App. LEXIS 20914, *16 (Fed. Cir. August 16, 2006), *quoting Enzo Biochem*, 323 F.3d at 964.

Since *Enzo Biochem*, the Court has issued a number of decisions applying the written description guidelines to claims to genetic material. These decisions provide additional guidance in determining compliance with the written description requirement and indicate that there is no per se rule of disclosure of precise structure for generic DNA-related claims. *See e.g., Monsanto*, 2006 U.S. App. LEXIS 20914; *Capon v. Eshhar*, 418 F.3d 1349 (Fed. Cir. 2005) (written description for generic invention need not reiterate the structure for the nucleotide sequences of the claimed chimeric genes); *Invitrogen Corp. v. Clontech Labs*, 429 F.3d 1052 (Fed. Cir. 2005) (written description sufficient where specification recited both DNA and amino acid sequences of a representative embodiment of a claimed protein); *Noelle v. Lederman*, 355 F.3d 1343, 1349 (Fed. Cir. 2004) (if human form of particular antigen had been disclosed, antibody could have been claimed by simply reciting its binding affinity for the "fully characterized" antigen).

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In the Office Action dated April 21, 2005, the Office rejected then-pending claims for lack of written description. The Office commented that "given the undefined and apparently unlimited nature of the claimed polynucleotides, it is apparent that the immunogenic functions of the undefined and claimed polynucleotides are not limited to an immunogenic composition that, for example, stimulates an immune response against a polynucleotide encoding SEQ ID NO:2. *The claims read on an undefined immune response to [a polypeptide encoded by] an undefined polynucleotide sequence.*" Office Action, paragraph spanning pages 11-12.

As Applicants understand these comments, the Office believed the prior claims could be interpreted as encompassing *any* nucleic acid that encoded a polypeptide sequence that can elicit an immune response against itself. The concern is apparently that the ability to elicit an immune response is a property of virtually all polypeptides and a claim so interpreted might be overbroad. These comments also suggested that the Office may have been analogizing to claims to expressed sequence tags (ESTs) in which neither the entire sequence of a gene nor the biological activity of the encoded protein is disclosed.

Applicants believe the claims submitted in this response avoid the issues previously raised by the Office. The claims recite compositions containing a nucleic acid that encodes a polypeptide consisting of, or comprising, an hTRT sequence (SEQ ID NO:2), wherein the compositions elicit an adaptive immune response to hTRT (SEQ ID NO:2). The polynucleotides of the claimed composition are therefore defined both by structure (consisting of or comprising SEQ ID NO:2) and correlated function (eliciting an adaptive immune response to SEQ ID NO:2). The claims now pending clarify that the immune response is against *hTRT*, and is elicited by the hTRT encoding sequence of the claimed composition. The immune response recited in the claims is "defined," and permits one of skill in the art to recognize the polynucleotides encompassed in the claimed composition.

In the new claims, the polynucleotide sequences (and the polypeptides they encode) are defined by the disclosure of SEQ ID NO:1 and SEQ ID NO:2, polypeptide

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fragments, variants, fusion proteins, and nucleic acids and vectors encoding them. The claimed hTRT sequences define "structural features commonly possessed by members of the genus that distinguish them from others." Disclosure of the precise structure of every possible polynucleotide fragment encoding a polypeptide fragment of hTRT is not required. *See Lizardtech, Inc. v. Regents of the University of California.*, 424 F.3d 1336, 1345 (Fed. Cir. 2005) (to comply with written description requirement, embodiments of the specification need not contain examples explicitly covering the full scope of the claim language). The written description is sufficient if one of skill in the art is persuaded that the inventor possessed the invention. *Id.*

Similarly, polypeptides including segments encoded by flanking sequences (portions of the polypeptide not corresponding to SEQ ID NO:2) encompassed by the claims are sufficiently supported not only by the written description, but also by the knowledge of one skilled in the art. Examples of such sequences are disclosed in the specification and one of skill in the art could readily envision a number of additional polypeptide sequences that could be linked to a fragment or the full sequence of hTRT.

In the currently pending claims, the immune function also is "defined," specific, and correlated to the disclosed structure of the hTRT sequence. Applicants incorporated the Examiner's suggestion and the claims now recite that the composition elicits an adaptive immune response to hTRT (SEQ ID NO:2). Moreover, the function is particular to the subject matter claimed and is not applicable to a broad class of invention.[3] Such functional descriptions of genetic material meet the written description requirement if "coupled with a known or disclosed correlation between function and structure." *Enzo*, 323 F.3d 956, 964 (Fed. Cir. 2002). Applicants have disclosed the entire polynucleotide sequence encoding hTRT (SEQ ID NO:1) and the entire amino acid sequence of hTRT(SEQ ID NO:2), coupled with a disclosed correlation between the function and that disclosed structure. Thus, one of skill in the art can envision the structure of the claimed compositions by the combination of structure and function

[3] Such a use is particular to the claimed compositions, and also satisfies the utility requirement under §101/§ 112.

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disclosed here. *See University of Rochester v. G.D. Searle & Co., Inc.*, 358 F.3d 916, 926 (Fed. Cir. 2004) (purpose of disclosing partial structure correlated with function is to permit one of skill in the art to deduce the structures of the claimed compositions); *Wallach*, 378 F.3d at 1359 (relationship between nucleic acid molecule's structure and its function in encoding a particular amino acid sequence is example of structure correlated with function).

In the April 21, 2005 Office Action, the Office also rejected previous claims in light of *Regents of the University of California v. Eli Lilly*. The Office stated, "The instant disclosure of a single species of polynucleotide does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera. The findings in *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1569 (Fed. Cir. 1997) are appropriate to the instant rejection....Given that the specification describes only SEQ ID NO:1, polynucleotide encoding SEQ ID NO:2, it is clear that a representative number of species falling within the genus is not provided." Office Action at page 11, second paragraph.

Lilly is not applicable to the pending claims for at least three reasons. First, the nature of the invention underlying the present claims is the nucleic acid compositions that elicit an immune response to hTRT. The entire hTRT gene has been disclosed by the inventors and the hTRT protein cloned and characterized in detail. In contrast, in *Lilly*, the claims were directed to gene sequences not disclosed in the specification. Second, the present claims do not define a genus of nucleic acids by function but rather by a combination of structure and function correlated to that structure. Such a disclosure is sufficient under current written description precedent. Finally, to the extent the present claims are open to the presence of additional polypeptide sequences by virtue of the term "comprising," one of skill in the art can easily envisage a number of representative examples of sequences that could be present. One of skill in the art knows that the disclosed KLH is a member of a class of molecules known as carrier proteins (sequences that enhance an adaptive immune response to sequence to which they are conjugated or fused). Disclosing known DNA/polypeptide structures is not

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necessary to demonstrate to a person of ordinary skill in the art that Applicants were in possession of the claimed invention.

More importantly, the substantial variability in the additional polypeptide sequences has nothing to do with the inventive contribution made by Applicants. The specification discloses a common structural feature shared by members of the claimed genus, which constitutes a substantial portion of the claimed genus. The claims are drawn to a genus that contains a nucleic acid that encodes hTRT or a fragment thereof (SEQ ID NO:2). One of skill in the art can readily envisage nucleic acid sequences that include the polynucleotide that encodes SEQ ID NO:2. Although there may be substantial variability among the species of compositions encompassed in the scope of the claims because SEQ ID NO:2 may be combined with sequences known in the art, e.g., expression vectors, KLH, the necessary common attribute is the polynucleotide encoding SEQ ID NO:2. Weighing all factors, including (1) that the full length polynucleotide sequence (SEQ ID NO:1), the full length polypeptide sequence of hTRT (SEQ ID NO:2), and the function of eliciting an immune response to hTRT (SEQ ID NO:2) are disclosed, (2) that any substantial variability within the genus arises due to the addition of elements that are not part of the inventor's contribution, and (3) in view of the knowledge and skill in the art, one skilled in the art would recognize from the disclosure that Applicants were in possession of the genus of the claimed compositions.

Here, Applicants have defined a genus of nucleic acid sequences in which the inventive and distinguishing features are defined by structure with correlated function, and for which representative examples of additional flanking sequences to which the claims are open (by virtue of the transitional phrase "comprising") are known and can readily be envisaged. Such a genus is of a scope appropriate to the invention disclosed by the application, an invention which is entirely different from that of *Lilly*. To find that an applicant is required to disclose every example of a flanking sequence (or corresponding polypeptide sequence) which the claims might encompass would be an impossible and unreasonable burden and at odds with current written description precedent. "The written description requirement states that the patentee must describe

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the invention; it does not state that every invention must be described in the same way." *Falkner v. Inglis*, 448 F.3d 1359, 1368 (Fed. Cir. 2006).

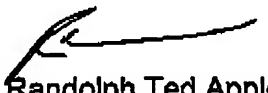
Applicants respectfully request that the Examiner consider the scope of each claim separately in determining whether the written description is sufficient. *See Capon*, 418 F.3d at 1357 (to determine compliance with written description requirement, the scope of each claim should be considered separately).

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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